

Serial No.: 09/477,082
Filed: December 30, 1999
Group Art Unit: 1642

This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS:

Claim 1 (canceled)

Claim 2 (currently amended): A method for detecting inactivation of a *CASP8* gene expression in a primary cancer cell, comprising detecting the absence of expression of a CASP8 protein.

Claim 3 (previously presented): The method according to claim 2, wherein the absence of expression of a CASP8 protein is detected by a method selected from the group consisting of immunoassay and biochemical assay.

Claims 4-10 (canceled)

Claim 11 (currently amended): The method according to claim 51 or 63, wherein the cancer is a tumor in which a *myc* gene is amplified.

Claim 12 (currently amended): The method according to claim 51 or 63, wherein the cancer is a neuroblastoma.

Claim 13 (currently amended): The method according to claim 51 or 63 ~~A method for diagnosis or prognosis of a cancer comprising detecting inactivation of a *CASP8* gene~~

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~~expression~~, wherein said method comprises detecting the absence of expression of a CASP8 protein.

Claim 14 (previously presented): The method according to claim 13, wherein the absence of expression of a CASP8 protein is detected by a method selected from the group consisting of immunoassay and biochemical assay.

Claim 15 (currently amended): The method according to claim 51 or 63 ~~A method for diagnosis or prognosis of a cancer comprising detecting inactivation of a CASP8 gene expression~~, wherein said method comprises detecting a methylation of *CASP8* genomic DNA.

Claim 16 (previously presented): The method according to claim 15, wherein the methylation of *CASP8* genomic DNA is detected by methylation polymerase chain reaction (PCR) assay.

Claims 17-28 (canceled)

Claim 29 (currently amended): A kit for detecting inactivation of a CASP8 gene expression, comprising ~~The kit of claim 27, wherein the detection assay comprises~~ oligonucleotide ~~PCR~~ primers for amplification of at least a part of the 5' untranslated region of *CASP8* genomic DNA, wherein said primers are used in a methylation polymerase chain reaction (PCR) assay.

Claims 30-47 (canceled)

Claim 48 (currently amended): A method for detecting inactivation of a *CASP8* gene expression in a primary cancer cell, comprising performing on the cancer cell at least one assay selected from the group consisting of detecting a methylation of *CASP8* genomic DNA, detecting the absence of expression of a *CASP8* protein, and detecting the absence of a *CASP8* mRNA.

Claim 49 (currently amended): A method for detecting inactivation of a *CASP8* gene expression in a primary cancer cell, comprising detecting the absence of a *CASP8* mRNA.

Claim 50 (previously presented): The method according to claim 49, wherein the absence of a *CASP8* mRNA is detected by a method selected from the group consisting of Northern blotting and reverse transcriptase-polymerase chain reaction (RT-PCR) assay.

Claim 51 (currently amended): A method for diagnosis ~~or prognosis~~ of a cancer comprising detecting inactivation of a *CASP8* gene expression in a cell from a subject, wherein said inactivation of a *CASP8* gene expression in the cell is indicative of the presence of a cancer and wherein said method comprises at least one assay selected from the group consisting of detecting a methylation of *CASP8* genomic DNA, detecting the absence of expression of a *CASP8* protein, and detecting the absence of a *CASP8* mRNA.

Claims 52-53 (canceled)

Claim 54 (previously presented): The method according to claim 48, wherein the inactivation of a *CASP8* gene expression is selected from the group consisting of homozygous deletion, heterozygous deletion coupled with gene silencing by methylation, and homozygous gene silencing by methylation.

Claim 55 (canceled)

Claim 56 (currently amended): A method for detecting inactivation of a *CASP8* gene expression in a primary cancer cell, comprising detecting a methylation of *CASP8* genomic DNA.

Claim 57 (previously presented): The method according to claim 56, wherein the methylation of *CASP8* genomic DNA is detected by methylation polymerase chain reaction (PCR) assay.

Claim 58 (currently amended): The kit of claim 29, wherein the kit detection assay comprises oligonucleotide PCR primers for amplification of SEQ ID NO: 1 or SEQ ID NO: 2.

Claim 59 (currently amended): The kit of claim 58, wherein the kit detection assay comprises at least one oligonucleotide PCR primer selected from the group consisting of SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, and SEQ ID NO: 34.

Claim 60 (previously presented): The method according to claim 56, wherein the methylation occurs in the 5' untranslated region of *CASP8* genomic DNA.

Claim 61 (previously presented): The method according to claim 60, wherein the methylation occurs in sequences selected from the group consisting of SEQ ID NO: 1 and SEQ ID NO: 2.

Claim 62 (previously presented): The method according to claim 57, wherein the PCR assay utilizes at least one of the primer sequences selected from the group consisting of SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, and SEQ ID NO: 34.

Claim 63 (new): A method for prognosis of a cancer comprising detecting inactivation of a *CASP8* gene expression in a cancer cell from a subject, wherein said inactivation of a *CASP8* gene expression in the cancer cell is indicative of the inefficiency of apoptosis induced by activated death receptors, chemotherapeutic drugs, or irradiation, and wherein said method comprises at least one assay selected from the group consisting of detecting a methylation of *CASP8* genomic DNA, detecting the absence of expression of a *CASP8* protein, and detecting the absence of a *CASP8* mRNA.

Claim 64 (new): The method according to claim 51 or 63, wherein said method comprises detecting the absence of a *CASP8* mRNA.

Claim 65 (new): The method according to claim 64, wherein the absence of a *CASP8* mRNA is detected by a method selected from the group consisting of Northern blotting and reverse transcriptase-polymerase chain reaction (RT-PCR) assay.

For Examiner's convenience, presented below are pending claims as amended arranged in a logical order:

Claim 48 (currently amended): A method for detecting inactivation of a *CASP8* gene expression in a primary cancer cell, comprising performing on the cancer cell at least one assay selected from the group consisting of detecting a methylation of *CASP8* genomic DNA, detecting the absence of expression of a CASP8 protein, and detecting the absence of a *CASP8* mRNA.

Claim 54 (previously presented): The method according to claim 48, wherein the inactivation of a *CASP8* gene expression is selected from the group consisting of homozygous deletion, heterozygous deletion coupled with gene silencing by methylation, and homozygous gene silencing by methylation.

Claim 56 (currently amended): A method for detecting inactivation of a *CASP8* gene expression in a primary cancer cell, comprising detecting a methylation of *CASP8* genomic DNA.

Claim 60 (previously presented): The method according to claim 56, wherein the methylation occurs in the 5' untranslated region of *CASP8* genomic DNA.

Claim 61 (previously presented): The method according to claim 60, wherein the methylation occurs in sequences selected from the group consisting of SEQ ID NO: 1 and SEQ ID NO: 2.

Claim 57 (previously presented): The method according to claim 56, wherein the methylation of *CASP8* genomic DNA is detected by methylation polymerase chain reaction (PCR) assay.

Claim 62 (previously presented): The method according to claim 57, wherein the PCR assay utilizes at least one of the primer sequences selected from the group consisting of SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, and SEQ ID NO: 34.

Claim 2 (currently amended): A method for detecting inactivation of a *CASP8* gene expression in a primary cancer cell, comprising detecting the absence of expression of a *CASP8* protein.

Claim 3 (previously presented): The method according to claim 2, wherein the absence of expression of a *CASP8* protein is detected by a method selected from the group consisting of immunoassay and biochemical assay.

Claim 49 (currently amended): A method for detecting inactivation of a *CASP8* gene expression in a primary cancer cell, comprising detecting the absence of a *CASP8* mRNA.

Claim 50 (previously presented): The method according to claim 49, wherein the absence of a *CASP8* mRNA is detected by a method selected from the group consisting of Northern blotting and reverse transcriptase-polymerase chain reaction (RT-PCR) assay.

Claim 63 (new): A method for prognosis of a cancer comprising detecting inactivation of a *CASP8* gene expression in a cancer cell from a subject, wherein said inactivation of a *CASP8* gene expression in the cancer cell is indicative of the inefficiency of apoptosis induced by activated death receptors, chemotherapeutic drugs, or irradiation, and wherein said method comprises at least one assay selected from the group consisting of detecting a methylation of *CASP8* genomic DNA, detecting the absence of expression of a *CASP8* protein, and detecting the absence of a *CASP8* mRNA.

Claim 51 (currently amended): A method for diagnosis ~~or prognosis~~ of a cancer comprising detecting inactivation of a *CASP8* gene expression in a cell from a subject, wherein said inactivation of a *CASP8* gene expression in the cell is indicative of the presence of a cancer and wherein said method comprises at least one assay selected from the group consisting of detecting a methylation of *CASP8* genomic DNA, detecting the absence of expression of a *CASP8* protein, and detecting the absence of a *CASP8* mRNA.

Claim 11 (currently amended): The method according to claim 51 or 63, wherein the cancer is a tumor in which a *myc* gene is amplified.

Claim 12 (currently amended): The method according to claim 51 or 63, wherein the cancer is a neuroblastoma.

Claim 15 (currently amended): The method according to claim 51 or 63 ~~A method for diagnosis or prognosis of a cancer comprising detecting inactivation of a *CASP8* gene expression,~~ wherein said method comprises detecting a methylation of *CASP8* genomic DNA.

Claim 16 (previously presented): The method according to claim 15, wherein the methylation of *CASP8* genomic DNA is detected by methylation polymerase chain reaction (PCR) assay.

Claim 13 (currently amended): The method according to claim 51 or 63 ~~A method for diagnosis or prognosis of a cancer comprising detecting inactivation of a *CASP8* gene expression,~~ wherein said method comprises detecting the absence of expression of a *CASP8* protein.

Claim 14 (previously presented): The method according to claim 13, wherein the absence of expression of a *CASP8* protein is detected by a method selected from the group consisting of immunoassay and biochemical assay.

Claim 64 (new): The method according to claim 51 or 63, wherein said method comprises detecting the absence of a *CASP8* mRNA.

Claim 65 (new): The method according to claim 64, wherein the absence of a *CASP8* mRNA is detected by a method selected from the group consisting of Northern blotting and reverse transcriptase-polymerase chain reaction (RT-PCR) assay.

Claim 29 (currently amended): A kit for detecting inactivation of a *CASP8* gene expression, comprising ~~The kit of claim 27, wherein the detection assay comprises~~ oligonucleotide PCR primers for amplification of at least a part of the 5' untranslated region of *CASP8* genomic DNA, wherein said primers are used in a methylation polymerase chain reaction (PCR) assay.

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Claim 58 (currently amended): The kit of claim 29, wherein the kit ~~detection-assay~~ comprises oligonucleotide PCR primers for amplification of SEQ ID NO: 1 or SEQ ID NO: 2.

Claim 59 (currently amended): The kit of claim 58, wherein the kit ~~detection-assay~~ comprises at least one oligonucleotide PCR primer selected from the group consisting of SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, and SEQ ID NO: 34.